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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,164	08/24/2005	Rob Hooft Van Huijsduijnen	SLH-P01-002	2570

28120 7590 03/19/2008

ROPES & GRAY LLP
PATENT DOCKETING 39/41
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,164	HUIJSDUIJNEN ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-46,48,49,52,53,55-60,62 and 64* is/are pending in the application.

4a) Of the above claim(s) *26-46,48,49,55-60,62 and 64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on January 08, 2008 is acknowledged. Claims 26-26-46, 48-49, 52-53, 55-60, 62 and 64 are pending in this application.

Restriction

1. Applicant's election with traverse of Group 16 (claim 53) in the reply filed on January 08, 2008 is acknowledged. The traversal is on the ground(s) that the Dente et al reference sequence identified by the Examiner (EFYGTYGLP) does not anticipate the special technical feature of the instant application. Furthermore, the Markush groups present in the claims, the Examiner has not fully considered paragraph (B)(2), as cited in the part 4 of the Office Action. Applicant argues that (B)(2) states that all alternatives belong to a recognized class of chemical compounds (mimetics or functional derivatives thereof) and have the common property of treating or preventing a PTP mediated diseases. This is not found persuasive because the Markush groups present in the claims are patentably independent and distinct because the phosphopeptide comprising an amino acid consensus sequence claimed do not have a common structural element, except for the phosphorylated tyrosine at position 0, as described in the previous office action. If the common structural element only requires a phosphorylated tyrosine at position 0, then Dente et al reference would anticipate the instant claims. Further, the only core sequence that these consensus sequence has in common is YG. This is not a significant structural element. In paragraph (B)(2) states that "the words, 'recognized class of chemical compounds' mean that there is an expectation from the knowledge in

the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended results would be achieved." Again, if all phosphopeptide belong to the same chemical compounds, then Dente et al peptide sequence would anticipate the instant claimed invention. Therefore, unity of invention is broken. Furthermore, in regards to part 7 of the Office Action, Examiner meant that since the process claims belong to different category, the process claims are independent or distinct from the product/peptide claims. In regards to the species election, different types of cancer is patentably independent and distinct from PTP mediated disease, since not all types of cancer are infectious diseases (for example, instant specification paragraph [0014]). Therefore, all cancers (genus) do not belong to PTP (protein tyrosine phosphatase) mediated disease genus. Furthermore, the diseases claimed have different mechanisms and different cells are involved. For example, gastrointestinal cancer is patentably independent and distinct from diabetes because the mechanisms and the cells involved are different. Further, search for one would not lead to the other. Therefore, the unity of invention is broken.

The requirement is still deemed proper and is therefore made FINAL. Claims 26-46, 48-49, 55-60, 62 and 64 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claim 52 has been rejoined with claim 53, and claim 52 is examined only to the extent as it reads on claim 53. Claims 52 and 53 are examined on the merits in this office action.

Rejection-35 U.S.C. 112, 2nd

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 52-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 52 recites, "...or a peptidomimetic, a non-peptide mimetic or a functional derivative of said phosphopeptide" at the last line of the claim. It is unclear what types of peptidomimetics, a non-peptide mimetic or a functional derivative of the phosphopeptides are encompassed by these mimetics or derivatives. For example, it is unclear what types of modifications would be considered to be peptidomimetics, non-peptide mimetics and functional derivative.

5. Claim 53 recites, "...or a peptidomimetic, a non-peptide mimetic or a functional derivative of said phosphopeptide." It is unclear what types of peptidomimetics, a non-peptide mimetic or a functional derivative of the phosphopeptides are encompassed by these mimetics or derivatives. For example, it is unclear what types of modifications would be considered to be peptidomimetics, non-peptide mimetics and functional derivative.

Rejection-35 U.S.C. 112, 1st

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 52-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention aims at identification of synthetic phosphopeptides that act as "ideal" substrate for five different protein tyrosine phosphatases (PTPs), and treatment or prevention of these diseases utilizing the PTP peptide inhibitors, wherein the disease is cancer.

(2) The state of the prior art:

In regards to "preventing a cancers", Merck manual indicates that cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age. Furthermore, the Merck manual indicates that many cancers are curable if detected at an early stage, and long-term remission is often possible in later stages. However, cure is not always possible and is not attempted in some advanced cases in which palliative care provides better quality of life than vigorous but fruitless attempts at tumor eradication (see Merck manual, Introduction). Additionally, the Merck manual indicates that malignancy may lead to pain, wasting, neuropathy, nausea, anorexia, seizures, hypercalcemia, hyperuricemia, or obstruction…Death typically occurs as a result of sudden or progressive failure of one or multiple organ systems (see Merck manual, Clinical Aspects of Cancer). Furthermore, a complete history and physical examination may reveal unexpected clues early cancer (see Merck manual, Clinical Aspects of Cancer, Diagnosis).

Furthermore, the Merck manual indicates that Gastrointestinal stromal tumors (GIST) are tumors of GI tract, and some are caused by previous radiation therapy to the abdomen for other tumors. Tumors are slow growing and malignant potential varies from minimal to significant. Symptoms vary with location but include bleeding, dyspepsia, and obstruction. Diagnosis is usually by endoscopy, with biopsy and endoscopic ultrasound. Treatment is surgical removal. The tyrosine kinas inhibitor imatnib has been beneficial (see Merck manual, Gastrointestinal Stromal Tumors, p.1).

Additionally, the Merck manual indicates that symptoms and signs of stomach cancer are nonspecific, and patients and physicians alike tend to dismiss symptoms or treat the patient for acid diseases. Later, early satiety may occur if the cancer obstructs the pyloric region or if the stomach becomes nondistensible secondary to lintis plastica (see Merck manual, Stomach Cancer, 1st paragraph in "Symptoms and Signs"). Furthermore, the Merck manual indicates that treatment decisions depend on tumor staging and the patient's wishes...curative surgery involves removal of most or all of the stomach and perhaps the regional lymph nodes. The true extent of tumor spread often is not recognized until curative surgery is attempted (see Merck manual, Stomach Cancer, "Treatment").

Furthermore, arts indicate the difficulties in going from *in vitro* to *in vivo* for drug development for treatment of cancers. Auerbach et al (Cancer and Metastasis Reviews, 2000, 19: 167-172) indicates that one of the major problems in angiogenesis research has been the difficulty of finding suitable methods for assessing the angiogenic response. For example, the 96 well rapid screening assay for cytokinesis was developed in order to permit screening of hybridoma supernatants...*In vitro* tests in general have been limited by the availability of suitable sources for endothelial cells, while *in vivo* assays have proven difficult to quantitate, limited in feasibility, and the test sites are not typical of the *in vivo* reality (see p. 167, left column, 1st paragraph). Gura T (Science, 1997, 278(5340): 1041-1042, enclosed 1-6) indicates that "the fundamental problem in drug discovery for cancer is that the model systems are not predictive at all" (see p. 1, 2nd paragraph). Furthermore, Gura T indicates that the results of xenograft

screening turned out to be not much better than those obtained with the original models, mainly because the xenograft rumors don't behave like naturally occurring tumors in humans—they don't spread to other tissues, for example (see p. 2, 4th paragraph). Further, when patient's tumor cells in Petri dishes or culture flasks and monitor the cells' responses to various anticancer treatments, they don't work because the cells simply fail to divide in culture, and the results cannot tell a researcher how anticancer drugs will act in the body (see p. 3, 7th paragraph). Furthermore, Jain RK (Scientific American, July 1994, 58-65) indicates that the existing pharmacopoeia has not markedly reduced the number of deaths caused by the most common solid tumors in adults, among them cancers of the lung, breast, colon, rectum, prostate and brain (see p. 58, left most column, 1st paragraph). Further, Jain RK indicates that to eradicate tumors, the therapeutic agents must then disperse throughout the growths in concentrations high enough to eliminate every deadly cells…solid cancers frequently impose formidable barriers to such dispersion (see p. 58, bottom of the left most column continuing onto the top of the middle column). Jain RK indicates that there are 3 critical tasks that drugs must do to attack malignant cells in a tumor: 1) it has to make its way into a microscopic blood vessel lying near malignant cells in the tumor, 2) exit from the vessel into the surrounding matrix, and 3) migrate through the matrix to the cells. Unfortunately, tumors often develop in ways that hinder each of these steps (see p. 58, bottom of right most column). Thus, the art recognizes that going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve.

The art provide guidance as to how to treat/alleviate cancers, but do not provide guidance as how to how to determine individuals who are susceptible to cancers (intestine cancers).

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art:

Applicant's activity is based on the determination of predicting those who are susceptible to cancers (intestine or stomach cancers). Since the activity is based on determining the patient population that is susceptible to cancers, the predictability in the art is low. This is due to the fact that the art has recognized the difficulty in determining the patient population who are susceptible to cancers.

The claims do not identify the patient population, therefore, the claims imply that anyone can be protected against cancers. However, the Applicant has not shown who will be susceptible cancers. There are too many variables between the experimentation, thus, it clearly shows the unpredictability of the art.

With regards to the effect of amino acid substitution in a peptide or protein, the art is unpredictable.

Rudinger (Peptide Hormones, JA Parsons, Ed., 1976, 1-7) teaches that, "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by

painstaking experimental study" (see p. 6). Additionally, SIGMA states that with regards to design of peptide sequences that, "Even for relatively short sequences, there are essential and non-essential (or less important) amino acid residues, although the relative importance of the individual amino acid residues is not always easy to determine" (see p. 1). SIGMA further describes what effect some substitutions may have, rather than what effect they will have on hydrophobicity, secondary structure (which will affect tertiary and quaternary structure), and solubility.

With regards to prediction of the native conformation of a protein (structure), the art is unpredictable. Berendsen (Science, 1998, 282: 642-643) states, "The prediction of the native conformation of a protein of known amino acid sequence is one of the great open questions in molecular biology and one of the most demanding challenges in the new field of bioinformatics" (see p. 642). Furthermore, Berendsen states that "Folding to the stable native state [computationally] has not (yet) occurred, and the simulations do not contain any relevant statistics on the process. The real protein will fold and refold hundreds to thousands of times until it stumbles into the stable conformation with the lowest free energy. Because this hasn't happened (and couldn't happen) in the simulations, we still cannot be sure of the full adequacy of the force field" (see p. 642).

Further, the effects of a single amino acid substitution can have substantial effects on proteins in structure and/or function and are exemplified by the difference between hemoglobin (Hb) and abnormal hemoglobins, such as sickle-cell hemoglobin (HbS). Voet et al teaches that the mutant hemoglobin HbE [GluB8(26)β to Lys] has, "no clinical manifestations in either heterozygotes or homozygotes" (see p. 235). Further,

Hb Boston and Hb Milwaukee both have single point mutations which results in altered binding affinity and ineffective transfer from the Fe(III) to Fe(II) oxidation state. Conversely, a single point mutation in Hb Yakima results in increased oxygen binding by the heme core, and in Hb Kansas, the mutation causes the heme center to remain in the T state upon binding oxygen (rather than structurally rearranging to the R state) (see p. 236). Further, HbS is a single point mutation, Val to GluA3(6)β (see p. 236), which results in deformation and rigidity of the red blood cell. The mutation also provides protection against most malarial strains.

Given that one could not determine the structure of a protein computationally, and that the effect of amino acid substitution is unpredictable, it flows logically that one would be unduly burdened with experimentation to determine the effect of amino acid substitution(s) in a peptide or protein, with regards to structure, function, or physical/chemical properties. Therefore, making phosphopeptide having conservative substitutions, peptidomimetic, a non-peptide mimetic or a functional derivative of the phosphopeptide that has the same activity as the claimed peptide, one would be unduly burdened with experimentation to determine the effect of amino acid content, substitution(s), addition and deletions in a peptide or protein, with regards to structure, function, or physical/chemical properties.

(5) The breadth of the claims:

The claims are drawn to a treating or preventing cancer, comprising administering to a patient in need thereof a pharmaceutically effective amount of a

phosphopeptide wherein the phosphopeptide comprises an amino acid consensus sequence (a), or a or a peptidomimetic, a non-peptide mimetic or a functional derivative of said phosphopeptide comprising an amino acid consensus sequence comprising amino acid positions –2, -1, 0, +1, +2, +3 and +4, wherein 0 is phosphorylated Y, -2 is selected from E, L and V, -1 is selected from a hydrophobic amino acid, +1 is G, +2 is A, T and S, +3 is selected from a hydrophobic amino acid and phenolic amino acid, and +4 is selected from A and G. The claim identifies the patient population as "a patient in need thereof", so they imply that everyone can be prevented from cancers.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

The specification does not provide guidance as when to administer the peptide composition in order to prevent cancer (intestine or stomach). The overview of the experiments indicates that phages were selected by immobilized, substrate trapping GST-PTP fusion proteins. After multiple rounds of selection, individual clones were confirmed by ELISA and SPOT analysis, and the sequence encoding the critical peptide displayed was subcloned and expressed in bacteria, and the resulting protein was used as a substrate for the wild-type version of the PTP; catalytic domain crucial for substrate recognition was identified (see paragraph [0146]). The specification discloses that a PTP1B trapping mutant was used as a positive control to validate the use of a phage display library to study substrate recognition. After three pannings of the tyrosine-biased library, an enrichment of binding phages was observed, and these were sequenced in

order to find a conserved motif (see paragraphs [0173]-[0174]). The specification further discloses phage display on PTP Sap1 and PTP-b, the sequence analysis of the phage display of these two subfamilies (see paragraph [0184]). Paragraph [0184] indicates that the phosphatase seems to be less efficient in the catalysis assay, dephosphorylation of the GST-peptide was weak (data not shown) as compared to the same experiment on PTP-Sap1. SPOT analysis on the positive clones of PTP-Sap1 indicates that there are three selective positions (-2, -1, +1) that can not be replaced by a Val and which seem to be restricted to their structure (see paragraph [0190]). The working example describes how to make the phage display, sequence these phage displays and test the amino acid sites that are important for phosphorylation/desphosphorylation. However, the working examples do not describe how to determine the patient population, and how to treat or prevent cancers in the patient population. There are no examples of testing these peptide compositions on cancers for prevention or treatment of intestine or stomach cancers. The specification discloses that these peptides can serve as highly specific inhibitors for the respective phosphate substrates, and are therefore useful in those diseases, in which inhibition of the respective phosphates is required.

As described supra, the Merck manual indicates that cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age. Furthermore, the Merck manual indicates that many cancers are curable if detected at an early stage, and long-term remission is often possible in later stages. However, cure is not always possible and is not attempted in

some advanced cases in which palliative care provides better quality of life than vigorous but fruitless attempts at tumor eradication (see Merck manual, Introduction). Additionally, the Merck manual indicates that malignancy may lead to pain, wasting, neuropathy, nausea, anorexia, seizures, hypocalcaemia, hyperuricemia, or obstruction…Death typically occurs as a result of sudden or progressive failure of one or multiple organ systems (see Merck manual, Clinical Aspects of Cancer). Furthermore, a complete history and physical examination may reveal unexpected clues early cancer (see Merck manual, Clinical Aspects of Cancer, Diagnosis).

Furthermore, the Merck manual indicates that Gastrointestinal stromal tumors (GIST) are tumors of GI tract, and some are caused by previous radiation therapy to the abdomen for other tumors. Tumors are slow growing and malignant potential varies from minimal to significant. Symptoms vary with location but include bleeding, dyspepsia, and obstruction. Diagnosis is usually by endoscopy, with biopsy and endoscopic ultrasound. Treatment is surgical removal. The tyrosine kinas inhibitor imatnib has been beneficial (see Merck manual, Gastrointestinal Stromal Tumors, p.1). Additionally, the Merck manual indicates that symptoms and signs of stomach cancer are nonspecific, and patients and physicians alike tend to dismiss symptoms or treat the patient for acid diseases. Later, early satiety may occur if the cancer obstructs the pyloric region or if the stomach becomes nondistensible secondary to lintis plastica (see Merck manual, Stomach Cancer, 1st paragraph in "Symptoms and Signs"). Furthermore, the Merck manual indicates that treatment decisions depend on tumor staging and the patient's wishes...curative surgery involves removal of most or all of the

stomach and perhaps the regional lymph nodes. The true extent of tumor spread often is not recognized until curative surgery is attempted (see Merck manual, Stomach Cancer, "Treatment").

Furthermore, arts indicate the difficulties in going from *in vitro* to *in vivo* for drug development for treatment of cancers. Auerbach et al (Cancer and Metastasis Reviews, 2000, 19: 167-172) indicates that one of the major problems in angiogenesis research has been the difficulty of finding suitable methods for assessing the angiogenic response. For example, the 96 well rapid screening assay for cytokinesis was developed in order to permit screening of hybridoma supernatants...*In vitro* tests in general have been limited by the availability of suitable sources for endothelial cells, while *in vivo* assays have proven difficult to quantitate, limited in feasibility, and the test sites are not typical of the *in vivo* reality (see p. 167, left column, 1st paragraph). Gura T (Science, 1997, 278(5340): 1041-1042, encloses 1-5) indicates that "the fundamental problem in drug discovery for cancer is that the model systems are not predictive at all" (see p. 1, 2nd paragraph). Furthermore, Gura T indicates that the results of xenograft screening turned out to be not much better than those obtained with the original models, mainly because the xenograft rumors don't behave like naturally occurring tumors in humans—they don't spread to other tissues, for example (see p. 2, 4th paragraph). Further, when patient's tumor cells in Petri dishes or culture flasks and monitor the cells' responses to various anticancer treatments, they don't work because the cells simply fail to divide in culture, and the results cannot tell a researcher how anticancer drugs will act in the body (see p. 3, 7th paragraph). Furthermore, Jain RK (Scientific American,

July 1994,58-65) indicates that the existing pharmacopoeia has not markedly reduced the number of deaths caused by the most common solid tumors in adults, among them cancers of the lung, breast, colon, rectum, prostate and brain (see p. 58, left most column, 1st paragraph). Further, Jain RK indicates that to eradicate tumors, the therapeutic agents must then disperse throughout the growths in concentrations high enough to eliminate every deadly cells…solid cancers frequently impose formidable barriers to such dispersion (see p. 58, bottom of the left most column continuing onto the top of the middle column). Jain RK indicates that there are 3 critical tasks that drugs must do to attack malignant cells in a tumor: 1) it has to make its way into a microscopic blood vessel lying near malignant cells in the tumor, 2) exit from the vessel into the surrounding matrix, and 3) migrate through the matrix to the cells. Unfortunately, tumors often develop in ways that hinder each of these steps (see p. 58, bottom of right most column). Thus, the art recognizes that going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve.

The specification has not provided guidance in the way of a disclosure to how to determine individuals that need protection against cancers. There is no clear guidance as to how to determine the patient population, since cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age, and it is unclear who would develop cancers, more guidance is necessary. Since the prior art is still unclear as to who are susceptible to cancers, more guidance is necessary.

(8) The quantity of experimentation necessary:

Since it is uncertain to predict the patient population who are susceptible for cancers and rheumatoid arthritis, and the Applicant have not provided the appropriate time frame at which the compound should be administered, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the phosphopeptide would be effective in preventing cancers.

Please note that the term "prevent" in an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat" or "alleviate", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes)- including preventing such disorders as cancers (stomach and intestine cancers), which is clearly not recognized in the medical art as being totally preventable condition.

8. Claims 52-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is

claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when

accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a method of treating or preventing cancer wherein the phosphopeptide comprises an amino acid consensus sequence…or a peptidomimetic, a non-peptide mimetic or a functional derivative of said phosphopeptide. The generic statements a peptidomimetic, a non-peptide mimetic or a functional derivative of said phosphopeptide do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 52-53 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can form peptide bonds, and make up the

class of phosphopeptides. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic and other synthetic peptide or peptide-like molecule that can function as peptidomimetics, non-peptide mimetics and functional derivatives. The specification does not disclose what types of derivatives retain the phosphopeptide functionality.

The specification is limited to the peptide or peptide-like molecules that belong to the same class of protein, phosphopeptides with tyrosine at position 0 phosphorylated. The specification discloses the amino acids that can be conservatively substituted, for example, Gly, Ala, Ser, Thr, and Pro can be conservatively substituted for Ser (see table I). The specification further discloses that non-cleavable peptide mimetic can render a peptide more stable and thus more useful as a therapeutic (replacement of L-amino acid residue is a standard way of rending the peptide less sensitive to proteolysis

and more similar organic compounds other than peptides) (see paragraph [0105] and Table II). The specification indicates that the techniques for the synthesis and the development of peptide mimetics and other non-peptide mimetics are well known in the art (see paragraph [0106]). The specification discloses that functional derivatives of the phosphopeptides may also be conjugated to polymers in order to improve the properties of the peptide, such as the stability, half-life, bioavailability, tolerance by the human body, or immunogenicity...at least one moiety attached to one or more functional groups, which occur as one or more side chains of the amino acid residues (see paragraph [0109]) and indicates PEGylation at one functional group (see paragraph [0110]). The working examples describe introducing and testing mutants to the phage, and tested on ELISA and SPOT analysis for binding and specificity. The specification does not describe any other functional derivative, such as other conjugated peptide that increases the stability, half-life, bioavailability and immunogenicity, such as human serum albumin and other peptidomimetics, non-peptide mimetics that can form peptide bonds, or any other type of peptide or peptide-like molecule that act as phosphopeptides (such as peptides comprising Thr, Ser and any other amino acid residues that may be phosphorylated). Description of conservative substitution, non-conservative substitution and functional conjugated peptide is not sufficient to encompass numerous other proteins and proteases that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. For example, there are 3 natural amino acids possible at position -2; 7 natural amino acids possible at position -1; 3 possible natural

amino acids possible at position 2; 7 natural amino acids possible at position 3; 2 natural amino acids possible at position 4. When the non-natural amino acids, amino acid mimetics, peptidomimetics and other conjugations are factored into the equation, the numbers increase exponentially. There are innumerable possibilities. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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